THE EFFECTIVENESS OF TRANQUILIZING DRUGS PLUS SUPPORTIVE PSYCHOTHERAPY IN TREATING BEHAVIOR DISORDERS OF CHILDREN: A DOUBLE-BLIND STUDY OF EIGHTY OUTPATIENTS*

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PSYCHOPHARMACOLOGIC agents, as tools of investigation and as means of therapy, have a potential of great importance in pediatric psychiatry (1–3). Freedman's excellent comprehensive review (4) has emphasized the tentative state of present knowledge, most reports being limited to initial clinical impressions (5). Yet there are already indications that indiscriminate usage has become a problem in pediatric practice (6). The pediatric literature as of April 1958, according to a bibliography prepared by the Psychopharmacology Service Center (7), consisted of 80 articles dealing with children and 54 which had at least passing reference to pediatric patients. We cannot here attempt a critical review of this literature. Most studies have dealt with institutionalized children, many of them defective, brain injured or psychotic. The few available publications on outpatients suffer from major limitations: inadequate controls, small numbers, failure to specify methodology, and insufficient attention to the effects of concurrent psychotherapy.

We were unable to find a study limited to emotionally disturbed nondefective pediatric *outpatients* that met the requisite standards of scientific rigor (8–10) evident, for example, in Freedman's inpatient study (11): namely, homogeneity of diagnostic categories, random assignment to treatment without knowledge by patient or physician of the drug to be administered to the individual patient, adequate specification of improvement criteria, and patient groups of a size adequate to permit statistical evaluation of outcome. Since our primary concern as clinicians has been with nonpsychotic emotionally disturbed children treated on an outpatient basis, we decided to attempt a controlled clinical study to compare the efficacy of short-term psychotherapy in conjunction with the administration of a propanediol derivative, meprobamate (Miltown); a phenothiazine, prochlorperazine (Compazine); and a placebo. The drugs were chosen to represent a mild and a strong tranquilizer of two different chemical classes.

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It had been our original intent to limit our study population to children with hyperkinetic behavior disorders on the hypothesis that tranquilizing drugs were likely to be of benefit to this diagnostic group. Although we had reason to anticipate an adequate referral rate, we shortly found ourselves confronted by a phenomenon common to clinical investigation: an unforeseen lag in referrals. We found it necessary to broaden intake to include the entire range of nonpsychotic disorders. Because of the consequent heterogeneity of the study population, procedures were established to permit separate evaluation of results in each diagnostic category in order not to confuse differences in prognosis with differences in treatment effects.

We therefore attempted to order the cases into serviceable diagnostic categories and established a quadripartite division for our purposes: neurotic, hyperkinetic, defective, and antisocial. The diagnosis of neurosis was made in those cases in which the manifestations of, or defenses against, anxiety were predominant, in accordance with APA nomenclature. The diagnosis of hyperkinetic behavior disorder was applied to children who were overactive, distractible, nonconforming, and disturbing to others, but who showed little or no anxiety. The diagnosis of mental deficiency with behavior disorder was made for children who had, among other signs of limited endowment, a Binet IQ of less than 80; these children had been referred for the behavior disorder but we felt that the mental defect itself was likely to play a role of sufficient importance in determining course so as to justify separate treatment of this group. The diagnosis of antisocial reaction was reserved for children with a history of repeated antisocial behavior and an attitude of indifference toward the social consequences of their acts.

Method

The subjects of this study were 83 children between the ages of 5 and 13, who were having problems in adjustment at home or at school. They were referred by school personnel, pediatric clinics and other community agencies to the Children's Psychiatric Service of the Johns Hopkins Hospital. Parents were told that psychiatric treatment and medication were to be offered, but were not told of the research function of the clinic. Professional fees for services rendered differed in no way from general hospital policies.

The mother's first interview with the social worker, 60 to 90 minutes in duration, was primarily devoted to an interpretation of the service, to history taking, and to evaluative procedures. A symptom check list, filled out with the mother, ensured uniform information concerning the behavior of the child and was checked at each subsequent visit as one means of determining progress. The child was seen by a pediatrician (with special training in child psychiatry) who evaluated the child's mental status and administered a short form Stanford-Binet Intelligence Test during his initial session with the

patient. At each subsequent clinic visit, the parent was seen by the social worker and the child by the pediatrician.

Sufficient capsules for a full course of therapy were set aside for each patient. At each visit a supply of medication sufficient to last until the next appointment was given to the mother. The capsules, containing meprobamate, prochlorperazine, or placebo, were identical in appearance. They were distributed in individual boxes numbered and coded by members of the Division of Clinical Pharmacology of the Department of Medicine at the Johns Hopkins Hospital;[1] the code was not broken until all judgments and evaluations were complete. Thus it was impossible for either therapists or patients to know what medication a particular patient received.

Parents were told that the capsules contained a tranquilizing drug that had been found to help children with similar problems. The proper dosage was explained carefully together with an interpretation of the importance of regular and sustained administration. In subsequent interviews mothers reported when and how the capsules were taken; the fact that the occasional missed dose was reported to us and tallied with the count of remaining capsules left us confident that instructions were followed faithfully in almost every instance.

The parents were told that the capsules were to make the patients "feel better," "to make the world seem happier," during which time, with psychotherapeutic help, new and more satisfying behavior patterns could be established. It was further explained that these patterns, because they were more satisfying, could be expected to continue after medication had been discontinued, since the parents would by then have acquired greater understanding of the basic problems. Part of the treatment goal with parents was directed at increased cooperation between the family and the school.

Interviews of one half to three quarters of an hour were planned at predetermined intervals of one, three, seven, and eleven weeks after the initial interview. During each a progress report was obtained. Therapy with parent and child was individualized for each family and was determined by our judgment of the nature of the problem and the ability of the child and parent to utilize one or another mode of therapeutic relationship. Where indicated, other community resources were called upon to assist in the treatment plan. Environmental changes, such as a readjustment of inappropriate school placements, were recommended and often effectuated during the period of therapy. Although the therapy with the family primarily involved the mother or mother substitute, fathers as well were seen whenever possible. Throughout the entire study, only one social worker and one physician were

[1] We would like to express our appreciation of the advice and assistance unstintingly given to us by Drs. Louis Lasagna, Victor Laties, and Bernard Weiss.

involved, so that the quality of treatment and any bias in judgment remained constant.

The drugs were dispensed by the social worker. The initial dosage prescribed was two capsules twice a day (morning and late afternoon); if there had been no change or insignificant improvement reported on the previous dosage, this was increased to two capsules three times a day at 1 week, and to two capsules four times a day at 3 weeks. The dosage of meprobamate ranged between 800 and 1600 mg., and that of prochlorperazine between 20 and 40 mg., per day. At 7 weeks medication was stopped so that the 11-week interview served to provide information on the response after the drug had been discontinued. A follow-up telephone call to the home six months later provided information about the patients' status at that time.

At 11 weeks a telephone call was placed to the teacher or school social worker of each patient. A progress report was obtained centering about academic achievement, behavior and social adjustment. An effort was made to determine whether the absence of medication during the last 4-week period had influenced progress.

In an effort to test yet another drug, perphenazine (Trilafon), 22 children who failed to improve significantly or who failed to sustain improvement during the period from the seventh to the eleventh week (when they were no longer taking the original medication) were given perphenazine or matching placebo capsules for an additional four-week period. The parents were told that this was a new drug which we expected to be stronger and more effective.

Judgment of improvement was made prior to knowledge of the distribution of medication. A child was considered to be significantly improved only when symptomatic change was sufficient to enable him to effect a more satisfying over-all interpersonal adjustment. Mild improvement was defined as some amelioration in symptoms without a meaningful change in adjustment. Significant improvement was scored as 2, mild improvement as 1 and no change or worse as 0.

The patient's progress was scored separately in three areas: home (as reported by the mother to the social worker), school (as reported by the teacher), and clinic (as observed by the physician). The necessity for therapeutic collaboration between physician and social worker inevitably resulted in some contamination of home and clinic scores, although they were registered independently at the end of treatment. The score based on the school report was less likely to have been so influenced. The coefficients of correlation between these judgments are reported in Table 1.

A summary improvement score for each child was determined on the basis of the home, school, and clinic improvement scores. In those cases where a discrepancy existed among the scores, the clinical judgment of the staff pre-

TABLE 1. COEFFICIENTS OF CORRELATION BETWEEN IMPROVEMENT SCORES

Doctor and social worker	0.60*
Doctor and teacher	0.68*
Social worker and teacher	0.52*

* Each of these correlations is significant at better than the 0.01 level.

vailed in assigning a summary score. A comparison of the results obtained on the basis of the summary scores with those obtained by taking simple arithmetic means of the three scores for each child yielded no significant changes in the data.

Results

Only 6 of the 83 children who began treatment dropped out before the 7-week evaluation. Three of the drop-outs were on placebo, two on meprobamate, one on prochlorperazine. All were hyperkinetic. The drop-out rate was gratifyingly small (7%) for an outpatient population; it suggests that a meaningful relationship was established with the participating families and indicates the feasibility of conducting outpatient drug studies.

The results on the 77 children who completed treatment are presented in Table 2.

There was no significant difference in outcome between placebo and the two drugs. However, for the reasons already specified, it is apparent that, in a heterogeneous population of disturbed children, outcome should be examined within each diagnostic group. The results of this analysis are presented in Table 3.

Although the number of cases in each subgroup is small, the outcome within each diagnostic category is similar and bears no evident relationship to drug action. Thus, with psychotherapy provided to all three treatment groups, we were unable to demonstrate any benefit from meprobamate or prochlorperazine over that conferred by placebo.

On the other hand, the nature of the psychiatric disorder itself proved to be a far more important variable in determining outcome than did the medication. If treatment subgroups are disregarded, the differences in mean im-

TABLE 2. SUMMARY IMPROVEMENT SCORES AT SEVEN WEEKS BY TREATMENT

	Placebo	*Meprobamate*	*Prochlorperazine*	*Total*
No. in group	25	24	28	77
Mean improvement score	1.32	1.17	0.89	1.07

TABLE 3. SUMMARY IMPROVEMENT SCORES AT SEVEN WEEKS BY DIAGNOSIS AND BY TREATMENT

Diagnosis	*Mean Scores by Medication*			
	Placebo	*Meprobamate*	*Prochlorperazine*	*Mean*
Neurotic	1.9 (9)	2.0 (4)	1.4 (8)	1.7 (21)
Hyperkinetic	1.2 (11)	1.1 (13)	1.1 (9)	1.1 (33)
Defective with behavior disorder	0.8 (4)	1.0 (3)	0.5 (6)	0.7 (13)
Antisocial	0.0 (1)	0.8 (4)	0.2 (5)	0.4 (10)
Total	1.3 (25)	1.2 (24)	0.9 (28)	1.1 (77)

(Numbers in parentheses represent the *N* for each group.)

provement scores between the neurotics and each of the other three diagnostic groups are statistically significant at the 0.05 level. The relationship between diagnosis and outcome is clearly evident in Table 4, in which the percentages of improvement are given for each diagnostic category without respect to medication.

Thus, 71 per cent of the neurotic patients showed significant improvement, whereas the corresponding figures for the hyperkinetic, defective and antisocial patients were 42 per cent, 23 per cent, and 10 per cent, respectively.

The regularity with which the neurotic children improved led us to the hypothesis that anxiety was particularly responsive to the treatment program. We then re-examined the hyperkinetic patients with the aid of staff members who did not know the outcome of these cases. We attempted to separate those children who might be considered constitutionally restless from those whose hyperkinesis might be secondary to anxiety. The results are presented in Table 5.

TABLE 4. IMPROVEMENT PERCENTAGES FOR EACH DIAGNOSTIC GROUP AT SEVEN WEEKS

Diagnosis	*Per Cent in Improvement Category*			*N*
	2	*1*	*0*	
Neurotic	71%	29%	0%	21
Hyperkinetic	42	21	36	33
Defective	23	23	54	13
Antisocial	10	20	70	10
	43%	23%	34%	77

TABLE 5. SUMMARY IMPROVEMENT SCORES AT SEVEN WEEKS FOR THE HYPERKINETIC CHILDREN

	Placebo	*Meprobamate*	*Prochlorperazine*	*Total*
"Constitutionally restless" Improvement mean	0.8 (4)	0.7 (6)	0.6 (5)	0.7 (15)*
"Secondarily hyperkinetic" Improvement mean	1.4 (7)	1.4 (7)	1.5 (4)	1.4 (18)*

* The differences between the two groups proved statistically significant at the 0.05 level.

Thus, the manifestations of anxiety proved to be strikingly responsive to the short-term treatment program, despite the fact that the symptoms were reported to have been present for no less than six months, most commonly about two years, prior to the onset of treatment.

A careful analysis of the data (Table 6) revealed that improvement was not correlated with patients' age, IQ, sex, color and family socioeconomic status.

An effort was also made to evaluate whether improvement could be correlated with the degree of disturbance in the parent who participated in the treatment program. This was done in retrospect, so that the results are not only subject to difficulties in scoring parental disturbance but are also probably colored in some measure by knowledge of the outcome of the treatment. It is, therefore, not surprising that we did indeed find that, as a group, the parents of the children who improved showed less basic personality disorder at the initial interview and a greater degree of response to the casework process.

Diagnosis and evaluation of improvement, while based on an over-all clinical picture of the patient's behavior at home and in the community, also

TABLE 6. SOCIAL CHARACTERISTICS OF PATIENTS IN RELATION TO IMPROVEMENT SCORE

Characteristic	*Improvement Category*		
	0	*1*	*2*
Mean age	8.8	9.3	9.0
Mean IQ*	100	99	101
% Boys	78	65	68
% White	65	75	71
Family economic level†	2.0	2.3	2.0

* Excluding defective cases.

† Socioeconomic Scale: 1 = under $2500; 2 = $2500–$6000; 3 = above $6000.

involved a close examination of the symptom inventory (Table 7) modified from Glidewell and others (12).

Eighty-one per cent of the children were described initially as having at least eight of these symptoms in varying degrees of severity, and 64 per cent, ten or more. The children who improved significantly had improved to some extent in almost all problem areas, rather than dramatically in one area alone. The only suggestive differences between placebo and drug appeared in two of the symptoms: sleep disturbance and temper. Both drugs appeared to

TABLE 7. SYMPTOM INVENTORY

List of Symptoms	
Problems of eating	Crying
Sleep disturbance	Lying
Enuresis	Stealing
Inability to get along with peers	Destructiveness
Inability to get along with adults	Fire-setting
Problems with siblings	Speech problems
Fears	Conversion symptoms
Tension or nervousness	Psychosomatic symptoms
Nailbiting or thumb-sucking	Tics and muscular spasticity
Restlessness	Immaturity
Masturbation and other sex problems	Emotional constriction
Temper outbursts	Obsessive-compulsive symptoms

be superior to placebo in controlling sleep disturbances, and prochlorperazine superior in controlling temper outbursts. These differences, however, are no more than suggestive, since they did not meet the statistical test of significance.

Toxic effects of medication were reported in 15 cases: 9 on prochlorperazine, 4 on meprobamate and 2 on placebo. In 12 of these cases the complaint was drowsiness, but in only 6 instances did the condition warrant a reduction in dosage. Of the 6 where cut-back was indicated, only 2 went below the original dosage level. Three of the mothers who complained were initially hostile to the idea of medication. Two children were described as staring and glassy-eyed; both of them had been receiving prochlorperazine. One child on two separate courses of placebo became "wild and unmanageable"; on each occasion the symptoms remitted when "medication" was discontinued. One child, after completion of study, was placed on prochlorperazine, 40 mg. per day. He developed painful torticollis which promptly disappeared when medication stopped and reappeared when medication was reinstituted. We were fortunate in not encountering the convulsive phenomena described by Shaw in patients on prochlorphenazine (13–15). Of the children who showed

toxic effects, 3 improved significantly, 6 showed mild improvement, and 6 remained unchanged. Their age distribution paralleled that for the total series (mean age 9 years).

At 11 weeks all those children not transferred to the perphenazine series were again evaluated to determine whether improvement had been sustained after medication was discontinued. Table 8 indicates that in those cases in which improvement had been achieved, it was indeed sustained after one month without drug or psychotherapy.

TABLE 8. SUMMARY IMPROVEMENT SCORES AT ELEVEN WEEKS

	Placebo	*Meprobamate*	*Prochlorperazine*	*Total*
Neurotic	1.7 (9)	2.0 (4)	1.6 (7)	1.8 (20)
Hyperkinetic	1.1 (8)	1.2 (9)	0.8 (6)	1.1 (23)
Defective with behavior disorder	0.7 (3)	1.5 (2)	0.7 (3)	0.9 (8)
Antisocial	0 (1)	0.8 (4)	0 (2)	0.4 (7)
Total	1.2 (21)	1.3 (19)	1.1 (18)	1.2 (58)

Nine children who were not significantly improved at the 7-week evaluation and 13 children who had failed to sustain their improvement at the eleventh week were placed upon perphenazine (12 to 16 mg. per day) or matching placebo for one month, again on a double-blind design and with random allocation to treatment. There were no toxic reactions of significance. While the numbers were small, there was a definite trend in favor of perphenazine over placebo. It is difficult to evaluate the significance of this difference in view of the fact that the perphenazine-treated group included more neurotic children than did the placebo group. We propose to examine the efficacy of perphenazine in a more exacting study in the future.

The use of treatment failures to test a second drug raises problems in the comparability of results. An unexpected finding in this series was the fact that the 13 children who had responded at first to the initial treatment but who had lost their gains by the eleventh week proved more refractory to the second treatment program (only 3 improved) than did the 9 who had shown no benefit from the initial treatment (7 improved on the second course).

The period of treatment for these patients, whether on one medication or two, had been quite brief. Although the positive results at seven weeks had been sustained by the eleventh week, it was of obvious interest to try to determine the durability of the benefit. At the end of a six-month interval from the last clinic visit, we called each parent after eliminating 5 children who had been institutionalized on our recommendation and one who had

been referred elsewhere for further treatment. Of the remaining 71 cases, we were successful in reaching 66.

Table 9 presents a comparison of 7-week, 11-week, and 6-month summary improvement scores for all patients. We have treated separately the 46 children who had only the first course of medication and the 20 who were placed on the perphenazine series after they failed to improve or lost their improvement during the first series.

The differences between diagnostic groups remained sharply evident at the

TABLE 9. COMPARISON OF 7-WEEK, 11-WEEK, AND 6-MONTH SUMMARY IMPROVEMENT SCORES FOR EACH DIAGNOSTIC GROUP

Diagnosis	*7-Week*	*11-Week*	*6-Month*	
			One Drug Series	*Two Drug Series*
Neurotic	1.7 (21)	1.8 (20)	1.9 (17)	1.7 (3)
Hyperkinetic	1.1 (33)	1.1 (23)	1.3 (18)	1.0 (10)
Defective	0.7 (13)	0.9 (8)	0.8 (5)	1.4 (5)
Antisocial	0.4 (10)	0.4 (7)	0.3 (6)	0.3 (2)
Total	1.1 (77)	1.2 (58)	1.3 (46)	1.1 (20)

six-month follow-up report. Ninety per cent of the neurotic children had either maintained their improvement or improved still further, a finding that was true of 68 per cent of the hyperkinetics and only 12 per cent of the antisocial children.

Comment

In order to appraise the significance of these findings, let us consider some of the questions of design and methodology that arise in relation to drop-outs, improvement indices, follow-up data, diagnostic categories and therapeutic implications.

How much bias has resulted from drop-outs? Six cases lost of a total of 83 represent only 7 per cent of the study population. All, however, had hyperkinetic behavior disorders. If all six cases had attained maximal improvement, the mean score for hyperkinetics would have risen to 1.2; if all had remained unimproved, it would have fallen to 1.0. In neither event would the change have obliterated the significance of the difference between the outcome of this group and that of the neurotic children. Three of the six were on placebo, two on meprobamate, one on prochlorperazine. If we select the assumption most favorable for the drugs, namely, that the first three may have shown no change and the second three maximal improvement, the difference between the mean scores for the treatment groups would have re-

mained within the range of random variation (placebo "1.0," meprobamate "1.3," and prochlorperazine "1.2"). We are therefore entitled to conclude that the results on the 77 patients who completed the program are representative of the response of the total study population.

How meaningful, reliable and sensitive are the improvement scores? Judging improvement on the basis of information obtained from the patient and his family is traditional practice in outpatient psychiatry; potentially, behavior research with children possesses an important advantage in that the school situation provides a standard screen against which deviations in performance can be measured (2). The school setting contains a built-in social control; the teacher of necessity judges the child against normative values determined by the peer group in his school district, which roughly corresponds to a fairly homogeneous socioeconomic sector. Teachers' judgments are of course influenced by training, experience and personality and cannot be expected to be constant between classrooms. We attempted to draw upon this valuable source of information about extramural social behavior by scoring teachers' reports.

Considerations of time, personnel and space precluded a direct assay of the reliability of each judge. The coefficients of correlation between scores do *not* represent a direct measure of this function. The doctor judged the behavior he observed in his office; the social worker judged the reports of behavior at home and at school. The correlation between scores, then, represents a measure of the covariance of clinic, home and school behavior. All of us are familiar with the child who is little or no problem at school but a major one at home, as well as the child who is the converse; in other words, we know that, while personality constellations indicate certain probabilities of response, the actual behavior in a given interpersonal setting is structured by the social field. The correlation coefficients reflect the degree of saturation of the behavior in each setting by this general factor of "personality." The inaccuracy of a judging method lowers apparent values from their "true" scores. Moreover, the constriction on measured covariance imposed by employing a three-point scale—0, 1, 2—for a continuously varying function tends once again to make the obtained correlations underestimates of the actual values. On the other hand, communication between mother and teacher, physician and social worker, has introduced an unknown contamination between judgments in the direction of increasing apparent covariance, despite our conscious efforts to minimize these effects.

With these stipulations in mind, we regard the correlation coefficients, varying from 0.52 to 0.68, but all significant, as an impressive confirmation of the meaningfulness of the scores we recorded. The composite score provides a more reliable measure of change than would have been obtained from limiting ourselves to behavior alterations in any single area. The sensitivity

of the method is attested to by the demonstration of significant differences in outcome between diagnostic categories and thus makes more meaningful the failure to demonstrate differences related to treatment program. Moreover, whatever the inherent error of the method, the double-blind design precluded systematic bias for or against any one of the medications.

To what extent can the 6-month follow-up scores be considered equivalent to the 7- and 11-week scores? Both 7- and 11-week ratings were based on the same method of clinical interview. The 6-month rating was limited to information obtained by phone from the mothers, in some instances supplemented by incidentally obtained reports from schools. We were concerned that improvement might be overestimated by a mother who was reluctant to portray the actual situation lest she be invited to return for further treatment. To counteract this factor, we made it standard practice to begin the conversation by explaining that we were terminating the service and were interested in checking out our results. The question still remains: to what extent may mothers be overly generous in estimating outcome, perhaps because they are grateful for services received or solicitous of the feelings of the clinic staff? We have no way of assessing this issue, a besetting problem in all follow-up studies of this nature which solicit cooperation from individuals whose set may be altered by the fact that they are no longer patients applying for help but are now independent of the clinic and are being appealed to in the name of research.

Are the impressive results to be ascribed to the treatment program? We had no untreated control group and cannot differentiate between "spontaneous" improvement and treatment results. Our findings, for the neurotic group, correspond to the usual results reported with outpatient psychiatric treatment of anxiety states (16–18). We are entitled to state that we failed to find a difference between the three treatment regimes. We can ascribe confidence to the findings in the neurotic and hyperkinetic categories in view of the size of the *N;* it is no more than a strong clinical impression in the defective and antisocial groups because of the small numbers of cases in each group.

However, the questions may properly be raised: Was the medication taken as prescribed? Was dosage adequate? Was a possible drug effect obscured by the ceiling imposed by the excellent results obtained from placebo plus psychotherapy? As to the first, we can only rely on the mother's report, usually quite scrupulous and in agreement with the tally of capsules the mother had left at the end of each period. As to the adequacy of dosage, we were operating in the range recommended for outpatients. The fact that side effects occurred in 13 of the 51 patients on tranquilizing drugs indicates that we were within the active range. Whether benefit would have been obtained by pushing dosage further we cannot state, but the impressive list of toxic

effects from both meprobamate and prochlorperazine in higher dosage ranges seems to us to contraindicate their use in this fashion with outpatients. The final question—Was a possible drug effect obscured by benefit accruing from psychotherapy plus placebo?—is indeed relevant in the case of the neurotic children. Since psychotherapy plus placebo resulted in an almost maximal improvement rate (1.9 out of a possible 2.0 points), even a highly effective drug could hardly be expected to demonstrate its value. With the shortage of trained personnel (19), it is meaningful to ask the question: Would either drug prove more effective than placebo if no psychotherapy were to be given? A study to answer this question poses major procedural difficulties; nonetheless, we hope to tease out an answer to this question in future investigations. There were, however, three diagnostic groups: hyperkinetic, defective, and antisocial, in which the benefits obtained from psychotherapy plus placebo left considerable room to register additional gains; in none did the drugs give evidence of greater usefulness. Parenthetically, we might comment on still another therapeutic issue. Is psychotherapy as effective without the act of administering placebo as it proved to be together with it? A study we are currently pursuing may provide an answer to this question.

Finally, what of the validity of the diagnostic categories? It requires no emphasis here that differences between clinicians in psychiatric diagnosis are so profound as to bring into doubt the usefulness of the present classification (20). We did not attempt subtle differentiations but relied on broad groupings. Nonetheless, there were inevitable differences of opinion within the staff. However, our diagnoses were recorded before the data were decoded and the major differences in outcome suggest the usefulness of the categories we employed. To some extent this may merely represent a prognostic judgment rather than a clinical distinction between syndromes. Nonetheless, there were apparently some factors in the presenting history and examination that did provide clues useful for differentiating cases. Our current study —restricted to children with neurotic and hyperkinetic behavior disorders— will serve as a further check of the validity of these diagnostic categories.

Above and beyond the significance of our findings for psychopharmacology, it seems to us that they have implications for public health practices. With a program of five interviews spaced over a three-month period, we obtained results with neurotic and, to some extent, hyperkinetic children that both initially and after six months compare favorably with the outcome reported in studies of more intensive outpatient psychotherapy. It is true that, in determining improvement, we emphasized change in the presenting complaint pattern rather than attempting to measure alterations in basic psychodynamic structure. There are, however, no reliable tools for assaying personality change and, unfortunately, no convincing studies that establish the

permanence of change resulting from intensive psychotherapy. At the present state of our knowledge it would seem justified to suggest, on the basis of this and other studies (21, 22), that community clinics re-evaluate their orientation toward treatment with the objective of increasing emphasis on evaluative consultations and short-term psychotherapy. In our hands, both have demonstrated their value in producing good clinical results for the populations described and under the conditions specified. Such an orientation permits a considerable extension of service to the community with the same clinical team.

One comment on a peripheral finding may be warranted. We were impressed by the fact that six months after the last clinic contact, seven of the ten mothers of defective children reported maintained or further improvement. In part, this may reflect diminution of management problems as maturation proceeds; in part it may reflect more adequate school programs. But it may also indicate greater acceptance by parents of their defective children as a delayed consequence (since initial results were disappointing) of the interpretation and support offered parents by the clinic. The behavior of the child may have changed with modifications in handling or may merely be better tolerated by more knowledgeable parents. If, however, one makes the assumption that no real change had occurred, it does by analogy cast doubt on the validity of the report of continuing improvement by the parents of the other children in the study population.

Finally, it should be stressed that the majority of our patients were from low socioeconomic strata (23, 24). Extrapolation from these findings to more privileged patients seen in private practice may not be warranted; only a study including such a group would answer this question.

Summary

Meprobamate, prochlorperazine, or placebo was administered to each of 83 children in a double-blind clinical trial. Concurrent psychotherapy was offered to each patient and his mother over a 3-month period at predetermined intervals. The children fell into four diagnostic categories: neurotic, hyperkinetic, defective with behavior disorder, and antisocial. Drop-out rate was gratifyingly small (7%) and confirmed the feasibility of conducting outpatient studies with children to evaluate psychiatric treatment. Outcome showed no relation to the medications used in this study. Placebo produced results equivalent to either drug. Outcome of treatment was influenced significantly by the nature of the presenting syndrome; neurotic children showed substantial improvement, hyperkinetic children moderate gains, and the other two groups little or none. Toxic reactions were mild. The lack of an untreated control group precluded any final judgment as to the role played by "spontaneous" improvement in the results observed. However, the symp-

tomatic improvement for this series of neurotic children and their parents, treated in 5 interviews over a 3-month period together with the administration of placebo capsules, proved to be of the same order as that described for more intensive programs of psychotherapy. These findings have public health implications.

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DISCUSSION

IRVIN A. KRAFT, M.D.:* It is a pleasure to discuss this paper. Most of my comments will be in the nature of amplifying well-taken points, ably made by the authors.

In their introduction they indicate the paucity of studies of outpatients. Work with children in such settings has many complications, and often these are not adequately considered in the design of the project. One of the greatest areas of need would seem to be in the psychiatric clinics for children, where long waiting lists prevail as the order of the day. Any study that offers insight into a therapeutic apparatus to deal more effectively with them is worthy of intense study and replication.

Our experience in a large school district bears out the difficulty of securing an adequate population for an outpatient study. The authors found 21 children in the neurotic group. It is interesting that the hyperkinetic group was the largest. It might be that the latter group is more likely to come to the attention of referral sources (parents, principals, teachers) than the first group.

Each mother filled out a symptom check list initially and at each visit. There are pitfalls to this procedure as we discovered in our study at Tulane. For example, if the investigator didn't cross-check the symptom list with the child, especially in the older age groups, there was the likelihood that a good deal of distortion by the mother would go undetected. Sometimes mothers painted a worse picture for certain reasons; other times they would gloss over something that would be picked up later from the child or another informant.

The authors assumed that the capsules were taken by the children. Again, to be skeptical, though not strongly so, we found that when some of our children were improving, the mothers then began taking the medication instead of the child. Again, one sometimes has to cross-check with the child to be sure he has taken the drug.

The authors are to be commended on utilizing community resources in their therapeutic endeavors. It tends to happen anyway, as when a mother discusses the clinic, the drug, the child and the doctor with her family advisers, neighbors and clinic companions.

One might comment that the quality of treatment probably did not re-

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main constant throughout the project. Presumably the setting of a study itself tends to focus and to sharpen the therapist. He also gains experience and may handle cases that enter the study at a later date in a more efficient manner. Whether this is truly significant is debatable.

I should like to raise one question, perhaps in a jocular vein, but nevertheless of value. Did the children taste the capsules? Some of our cases bit into the drugs and soon knew they had received a different pill (though alike in color, weight and size) from the first ones. This did affect some of our subjects and their parents.

The need for some objectification of observations is great. Apparently the authors feel they satisfactorily solved this problem since their correlations were statistically significant. The gratifying low drop-out rate is something that the authors should elaborate on. Since this factor so often vitiates studies, the more we know of good techniques to avoid it the better we can handle it.

In their results the placebo and the two drugs showed no significant differences. This is not unexpected in a situation such as is described in the paper. Often placebo administration has an improvement rate of 30 per cent or so regardless of diagnostic category. However, the authors show clearly that the diagnostic grouping was the significant factor. Placebo improvement in the latter two groups was not significant as compared with the neurotic and hyperkinetic groups.

The paper suggests that anxiety was "particularly responsive to the treatment program." Yet they do not find data to support the assumption that Thorazine and Compazine are truly anti-anxiety agents. Their data indicate that placebos are equally so, if one disregards psychotherapy, etc.

Improvement, when present in the children, tended to be in "all problem areas." This is consistent with our observations on children with school phobias, minor convulsive disorders and neurotic problems. Since a child is holistic in his adaptations, he would tend to continue to be so when under treatment. A further study of changes in family dynamics would be of interest. We might find a significant shift in family interactions as the child's behavior patterns change.

The authors are to be commended highly for an excellent paper. It adequately examines its own procedures, complications and results. They shed light on new possibilities of public health child psychiatry. This type of study and its results should be studied with interest by child-caring and child-treatment agencies.